

II. REMARKS

The Office Action dated November 28, 2005, has been received and carefully noted. The amendments made herein and the following remarks are submitted as a full and complete response thereto.

Claims 23-25, 27, 29, 31-66, 68-78 are pending in the present application. Applicants thank the Examiner for indicating that claims 25, 31-33, 35, 37-58, 63-66 and 68-72 are allowable. Claims 24, 27, 29, 34, 36, 59, 60, 62, and 74 are withdrawn from consideration by the Examiner. Applicants respectfully disagree with the Examiner's withdrawal of claim 36, because claim 36 was indicated as allowable in the June 16, 2005 Office Action (see page 2, lines 10-11) and Applicants did not request withdrawal of claim 36. Applicants request clarification from the Examiner as to the reason for the withdrawal. Applicants reserve the right to file one or more divisional applications to the subject matter of the withdrawn claims.

At this time, claims 24-25, 27, 29, 31, 34-38, 44, 47, 51, 53, 58-60, 62-66, 68-73, and 76 are amended. Support for the claim amendments can be found in the specification and claims as originally filed. In particular, claims 24, 25, 27, 29, 31, 34-38, 44, 47, 51, 53, 58-60, 62-65, 68-73, and 76 are amended to replace the word "having" with the word "of" in order to expedite prosecution of the present application. Further, additional amendments to claim 73 are supported, for example, by page 2, lines 1-34 of the specification and by the compound "SPA21" on page 30, line 10 of the specification. Therefore, Applicants believe that no new matter is added.

Claims 66 and 68 were characterized as "Currently Amended" in the Applicants' Response filed September 14, 2005. Applicants note that claim 66 was amended to add a "." at the end of the claim, but Applicants inadvertently failed to underline the "." to designate the amendment. In claim 68, no amendments had been made, and the claims were inadvertently labeled as "Currently Amended." Applicants apologize for the confusion.

Claim 73 was rejected under 35 U.S.C. § 112, second paragraph for the asserted indefiniteness. Applicants respectfully traverse this rejection in view of the preceding claim amendments and the succeeding remarks.

Applicants submit that this rejection has been rendered moot, in part, by the above amendments to claim 73. Claim 73 has been amended to correct the typographical error of the repetition of the phrase "having the formula" and to add the word "thereof" after the phrase "pharmaceutically acceptable salt," as suggested by the Examiner.

However, Applicants disagree with the Examiner's assertion that claim 73 is indefinite because it "mandates the presence of a second compound, while at the same time not identifying it" (Office Action, page 3, lines 18-19). In contrast, Applicants note that the last line of claim 73 discloses "and an acceptable pharmaceutical excipient." As such, claim 73 already identifies a second compound, as requested by the Examiner.

Accordingly, Applicants request reconsideration and withdrawal of the rejection of claim 73 under 35 U.S.C. §112, second paragraph.

Claims 23, 61, 73, and 76 were rejected under 35 U.S.C. §102(a) as being anticipated by Johnson et al. (WO 97/04004). Applicants respectfully traverse the rejection.

Applicants disagree with the Examiner's assertion that compound 26 of Johnson et al. "is encompassed by claims 23 and 61 when the substituent variables are as follows: ... R₂ = hydrogen; R₃ = methyl; R₄ = methyl;... Y = propylene substituted with isobutyl; Z = -O-CH₂-CH₃ " (Office Action, page 5, lines 1-6) (emphasis added). In contrast, claim 23 of the present invention discloses:

R₁ and R₂ are independently selected from the group consisting of: H, R, and ArR-, provided that neither R₁ or R₂ is tert-butoxycarbonyl, and provided that if either one of R₁ and R₂ is H, each of R₃, R₄, R₆ and R₈ are H and R₅ is isopropyl or phenyl...

(claim 23) (emphasis added). In other words, in claim 23, if R₂ is hydrogen, then R₃ and R₄ are not methyl.

Meanwhile, claim 61 of the present invention discloses that "R₉ is Y-COOH." In contrast, as noted by the Examiner, Y in the compound of Johnson et al. is "propylene substituted with isobutyl" (Office Action, page 5, line 11). Thus, Johnson et al. does not teach or suggest a -COOH group in the R₉ position in the compound of Johnson et al. Additionally, there is no Z group in claim 61 of the present invention, while in the compound of Johnson et al. there is a Z group of -O-CH₂-CH₃, as noted by the Examiner (Office Action, page 5, line 12).

Applicants submit that Johnson et al. does not teach or suggest a compound of present claim 73 for at least the same reasons as claim 23, as present claim 73 discloses that "if either one of R₁ and R₂ is H, each of R₃, R₄, R₆ and R₈ are H and R₅ is

isopropyl or phenyl....” (emphasis added). As in claim 23, claim 73 discloses that if R₂ is hydrogen, then R₃ and R₄ are hydrogen, not methyl.

In claim 76 of the present invention, “R₁ and R₂ are independently selected from the group consisting of: H, methyl, ethyl, propyl and n-butyl” (emphasis added). In contrast, “R₁ is benzoyl” in compound 26 of Johnson et al., as noted by the Examiner (Office Action, page 5, line 3) (emphasis added). Applicants submit that Johnson et al. does not teach or suggest a compound of present claim 76, as the R₁ group of Johnson is not H, methyl, ethyl, propyl, or n-butyl.

As Johnson et al. does not teach or suggest all of the elements of claims 23, 26, 73, and 76, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 23, 61, 73, and 76 under 35 U.S.C. § 102(a) over Johnson et al.

Claim 76 was rejected under 35 U.S.C. § 102(b) as being anticipated by Reetz (*Angew. Chem. Int. Ed. Eng.*, 31(12), 1626-9, 1992). Applicants respectfully traverse the rejection.

Present claim 76 discloses “[a] compound or pharmaceutically acceptable salt of the formula... wherein R₁ and R₂ are independently selected from the group consisting of: H, methyl, ethyl, propyl, and n-butyl” (emphasis added). In contrast, as the Examiner noted, Reetz discloses a compound in which “R₂ = tBoc” (Office Action, page 5, line 20) (emphasis added). As such, Applicants agree with the Examiner that present claim 76 “exclude[s] the possibility that R₂ (or R₁) can be *tert*-butyloxycarbonyl” as in Reetz. Reetz does not teach or suggest a compound in which R₁ and R₂ are hydrogen, methyl, ethyl, propyl, or n-butyl.

Therefore, as Reetz does not teach or suggest all of the elements of claim 76, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 76 under 35 U.S.C. § 102(b) over Reetz.

Claim 76 was rejected under 35 U.S.C. § 102(b) over Falender et al. (*Biocatal. Biotransform.*, 13(2), 131-139, 1995). Applicants respectfully traverse the rejection.

Present claim 76 discloses “[a] compound or pharmaceutically acceptable salt of the formula... wherein R₁ and R₂ are independently selected from the group consisting of: H, methyl, ethyl, propyl, and n-butyl...” (emphasis added). In contrast, as the Examiner noted, Falender et al. discloses a compound in which “R₁ = allylglycine” (Office Action, page 7, line 3). Applicants agree with the Examiner that claim 76 “excludes allylglycine as a possibility for R₁” (Office Action, page 6, lines 2-3). Further, Falender et al. does not teach or suggest that R₁ of present claim 76.

Applicants believe that the Examiner’s statement that “Claim 23 excludes allylglycine as a possibility for R₁” (Office Action, page 6, lines 2-3) (emphasis added) was a typographical error in which he meant to say “Claim 76 excludes allylglycine...,” as the rejections of claim 23 over Falender et al. were withdrawn (see Office Action, page 2).

Therefore, for at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 76 under 35 U.S.C. § 102(b) over Falender et al.

Claims 73 and 76 were rejected under 35 U.S.C. § 102(b) over Chang et al. (*Bioorg. Med. Chemistry Letters*, 2(10), 1207-12, 1992). Applicants respectfully traverse the rejection.

Present claim 73 discloses “[a] pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof, of the formula:... provided that if either one of R₁ and R₂ is H, each of R₃, R₄, R₆ and R₈ are H and R₅ is isopropyl or phenyl (emphasis added). In contrast, as the Examiner noted, Chang et al. discloses a compound in which “R₁ = hydrogen, R₂ = hydrogen,... [and] R₅ = –CO–NH₂...” (Office Action, page 8, lines 3-7) (emphasis added). Further, Applicants submit that Chang et al. does not teach or suggest that “R₅ is isopropyl or phenyl” when either one of R₁ and R₂ is hydrogen.

Meanwhile, present claim 76 also discloses “[a] compound or pharmaceutically acceptable salt thereof, of the formula...” Applicants submit that Chang et al. does not teach or suggest the substituents of claim 76. In contrast, Chang et al. discloses compounds with additional amino acids added to the N-terminus.

For at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 73 and 76 under 35 U.S.C. § 102(b) over Chang et al.

Claims 73 and 76 were also rejected under 35 U.S.C. § 102(e) over Webber et al. (U.S. Patent No. 6,214,799). Applicants respectfully traverse the rejection.

As noted above, present claim 73 discloses “[a] pharmaceutical composition comprising a compound or pharmaceutically acceptable salt thereof, of the formula... provided that if either one of R₁ and R₂ is H, each of R₃, R₄, R₆ and R₈ are H...” (emphasis added). In contrast, as noted by the Examiner, Webber et al. discloses a compound in which “R₆ = hydrogen, R₃ = hydrogen,... R₄ is alkyl, R₁ = hydrogen” (Office Action, page 9, lines 5-8) (emphasis added). In present claim 73, when R₁ is

hydrogen, R₄ is not alkyl. Webber et al. does not teach or suggest that R₄ is hydrogen when R₁ or R₂ is hydrogen.

Claim 76 discloses a “compound or pharmaceutically acceptable salt thereof, of the formula:..., wherein...R₅ is selected from the group consisting of: R, ArR-, and Ar-,” where “R is defined as a saturated or unsaturated moiety having a linear, branched, or non-aromatic cyclic skeleton containing one to ten carbon atoms...and Ar is an aromatic ring.” In contrast, as the Examiner noted, Webber et al. discloses a compound in which “R₅ = hydrogen” (Office Action, page 9, line 7) (emphasis added).

Additionally, claim 76 discloses that “R₁ and R₂ are independently selected from the group consisting of: H, methyl, ethyl, propyl and n-butyl” (emphasis added). In contrast, Webber et al. discloses a compound in which “R₂ = a benzyl group that is “substituted” with oxo (resulting in a benzoyl group)” (Office Action, page 9, line 10). Further, Webber et al. does not teach or suggest that R₂ is hydrogen, methyl, ethyl, propyl, or n-butyl. Thus, Webber et al. does not teach all of the elements of present claim 76.

For at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 73 and 76 under 35 U.S.C. § 102(e) over Webber et al.

Claims 75, 77, and 78 were rejected under 35 U.S.C. § 102(e) as being anticipated by Eisenbach-Schwartz et al. (U.S. Patent No. 6,126,939). Applicants respectfully traverse the rejection.

Present claim 75 discloses:

A compound or pharmaceutically acceptable salt thereof, of the formula:... wherein...Y is a linear, unsaturated, two to six carbon alkyl group, optionally substituted with phenyl, naphthyl, anthracyl, phenanthryl or a saturated or unsaturated moiety having a linear, branched, or non-aromatic cyclic skeleton consisting of one to ten carbon atoms optionally substituted with: =S, -OH...

(emphasis added).

In contrast, Eisenbach-Schwartz et al. discloses a compound in which “Y = ethyl,” as noted by the Examiner, (Office Action, page 9, line 24). Applicants respectfully disagree with the Examiner’s assertion that “Y can be a saturated moiety having linear or branched... skeleton containing 1-10 carbon atoms” (November 28, 2005 Office Action, page 10, lines 3-4) (internal quotes omitted). Although claim 75 includes the phrase “a saturated or unsaturated moiety having a linear, branched, or non-aromatic cyclic skeleton,” the phrase refers to what the “linear, unsaturated, two to six carbon alkyl group” is “optionally substituted with,” not the definition of Y itself (emphasis added). In contrast, Applicants respectfully submit that the “ethyl” of Eisenbach-Schwartz et al. is a linear, saturated, two carbon alkyl. Further, Eisenbach-Schwartz et al. does not teach or suggest substituent Y of present claim 75.

Further, Claims 77 and 78 are dependent on Claim 75. Applicants submit that Eisenbach-Schwartz et al. does not teach or suggest the compounds of claim 77 and 78 for at least the same reasons as claim 75, as claim 75 discloses that “Y is a linear, unsaturated, two to six carbon alkyl group” (emphasis added).

For at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 75, 77, and 78 under 35 U.S.C. § 102(e) over Eisenbach-Schwartz et al.

Claim 76 was rejected under 35 U.S.C. § 102(b) over Grubbs et al. (U.S. Patent No. 5,811,515). Applicants respectfully traverse the rejection.

Present claim 76 discloses:

A compound or pharmaceutically acceptable salt thereof, of the formula:..., wherein...

R₁ and R₂ are independently selected from the group consisting of: H, methyl, ethyl, propyl and n-butyl;...

R is defined as a saturated or unsaturated moiety having a linear, branched, or non-aromatic cyclic skeleton...

Z is defined as a moiety selected from the group consisting of: -OH; -OR; -SH; -SR; -NH₂; or pharmaceutically acceptable salt thereof

(emphasis added). In contrast, Grubbs et al., as noted by the Examiner, discloses a compound in which "R₁ = allylglycine; R₂ = tBoc;... Z = -O-CH₂-C₆H₅" (Office Action, page 10, lines 17-18). Grubbs et al. does not teach or suggest R₁, R₂ or Z of present claim 76.

Therefore, for at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 76 under 35 U.S.C. § 102(b) over Grubbs et al.

III. CONCLUSION

In view of the amendments and remarks above, Applicants respectfully submit that this application is in condition for allowance and request favorable action thereon. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to discuss any remaining issues.

Any additional fees that are required with respect to this response may be charged to Deposit Account No. 01-2300, referencing Attorney Docket No. 108281-00000.

Respectfully submitted,

ARENT FOX PLLC

A handwritten signature in black ink, appearing to read 'Richard J. Berman', with a large, loopy flourish extending to the right.

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Enclosure: Petition for Extension of Time (3 months)